Preclinical development of AAV vector-mediated in vivo hepatic reprogramming of myofibroblasts as a therapy for liver fibrosis

Grant Award Details

Preclinical development of AAV vector-mediated in vivo hepatic reprogramming of myofibroblasts as a therapy for liver fibrosis

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10088

Project Objective: Preclinical development of AAV vector-mediated in vivo hepatic reprogramming of myofibroblasts as a therapy for liver fibrosis.

Investigator:

Name:	Holger Willenbring
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Liver Disease

Award Value: $1,638,389

Status: Active

Grant Application Details

Application Title: Preclinical development of AAV vector-mediated in vivo hepatic reprogramming of myofibroblasts as a therapy for liver fibrosis

Public Abstract:

Research Objective

An intravenously injectable virus that converts the scar cells responsible for liver cirrhosis into the cells that provide most of the liver's function, thereby preventing or reversing liver failure.

Impact

The proposed research will develop a new therapy for liver cirrhosis, which can be cured by liver transplantation, but there are not enough donor organs for all patients in need.

Major Proposed Activities

- Construction of a single AAV vector expressing the human transcription factors FOXA3, HNF1A and HNF4A effective in hepatic reprogramming of human myofibroblasts.
- Identification of chimeric AAV capsids that transduce human myofibroblasts in vivo with high efficiency and specificity.
- Identification of human myofibroblast-targeted chimeric AAV capsids that are not neutralized by human antibodies against naturally occurring AAV capsids.
- Demonstration of therapeutic efficacy and principal safety of in vivo hepatic reprogramming of human myofibroblasts.

Statement of Benefit to California:

California has one of the longest wait times for a donor liver in the US. Therefore, many Californians with liver cirrhosis have to be hospitalized or die while waiting for a transplant. By developing a broadly applicable new therapy for liver cirrhosis, the proposed research will improve the outcomes of patients with liver cirrhosis and reduce the financial burden on California's medical system.

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